



UBE3A gene

ubiquitin protein ligase E3A

Normal Function

The *UBE3A* gene provides instructions for making a protein called ubiquitin protein ligase E3A. Ubiquitin protein ligases are enzymes that target other proteins to be broken down (degraded) within cells. These enzymes attach a small protein called ubiquitin to proteins that should be degraded. Cellular structures called proteasomes recognize and digest these ubiquitin-tagged proteins. Protein degradation is a normal process that removes damaged or unnecessary proteins and helps maintain the normal functions of cells.

Studies suggest that ubiquitin protein ligase E3A plays a critical role in the normal development and function of the nervous system. However, its exact role in nervous system cells is unclear.

People normally inherit two copies of the *UBE3A* gene, one from each parent. Both copies of the gene are turned on (active) in most of the body's tissues. In certain areas of the brain, however, only the copy inherited from a person's mother (the maternal copy) is active. This parent-specific gene activation results from a phenomenon known as genomic imprinting.

Health Conditions Related to Genetic Changes

Angelman syndrome

A loss of *UBE3A* gene function in the brain likely causes many of the characteristic features of Angelman syndrome, a complex genetic disorder that primarily affects the nervous system. This loss of function results from a chromosomal change or gene mutation that affects the maternal copy of the gene.

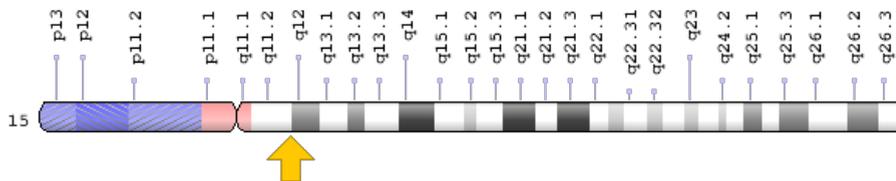
Several different genetic mechanisms can turn off (inactivate) or delete the *UBE3A* gene. Most cases of Angelman syndrome (about 70 percent) occur when a segment of the maternal chromosome 15 containing this gene is deleted. In another 11 percent of cases, Angelman syndrome results from mutations within the *UBE3A* gene itself. Most of these mutations lead to the production of an abnormally short, nonfunctional version of ubiquitin protein ligase E3A. Because the copy of the gene inherited from a person's father (the paternal copy) is normally inactive in some areas of the brain, loss of the maternal copy prevents any of the enzyme from being produced in these brain regions. This lack of enzyme function likely causes the major signs and symptoms of Angelman syndrome.

Other abnormalities involving the region of chromosome 15 that contains the *UBE3A* gene can also cause Angelman syndrome. These chromosomal changes include rearrangements (translocations) of genetic material or a defect in the region of DNA that controls activation of the *UBE3A* gene. Like mutations within the gene, these chromosomal changes prevent any functional ubiquitin protein ligase E3A from being produced in certain parts of the brain.

Chromosomal Location

Cytogenetic Location: 15q11.2, which is the long (q) arm of chromosome 15 at position 11.2

Molecular Location: base pairs 25,337,234 to 25,439,086 on chromosome 15 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ANCR
- CTCL tumor antigen se37-2
- E6-AP
- E6AP ubiquitin-protein ligase
- EPVE6AP
- HPVE6A
- human papilloma virus E6-associated protein
- oncogenic protein-associated protein E6-AP
- UBE3A_HUMAN
- ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Protein turnover is tightly regulated
<https://www.ncbi.nlm.nih.gov/books/NBK22397/>

GeneReviews

- Angelman Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1144>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28UBE3A%5BTIAB%5D%29+OR+%28ubiquitin+protein+ligase+E3A%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- UBIQUITIN-PROTEIN LIGASE E3A
<http://omim.org/entry/601623>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/UBE3AID42756ch15q11.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=UBE3A%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12496
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/7337>
- UniProt
<http://www.uniprot.org/uniprot/Q05086>

Sources for This Summary

- Bittel DC, Kibiriyeva N, Talebizadeh Z, Driscoll DJ, Butler MG. Microarray analysis of gene/transcript expression in Angelman syndrome: deletion versus UPD. *Genomics*. 2005 Jan;85(1):85-91.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15607424>
- Camprubí C, Guitart M, Gabau E, Coll MD, Villatoro S, Oltra S, Roselló M, Ferrer I, Monfort S, Orellana C, Martínez F. Novel UBE3A mutations causing Angelman syndrome: different parental origin for single nucleotide changes and multiple nucleotide deletions or insertions. *Am J Med Genet A*. 2009 Mar;149A(3):343-8. doi: 10.1002/ajmg.a.32659.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19213023>
- Clayton-Smith J, Laan L. Angelman syndrome: a review of the clinical and genetic aspects. *J Med Genet*. 2003 Feb;40(2):87-95. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12566516>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735357/>
- Fang P, Lev-Lehman E, Tsai TF, Matsuura T, Benton CS, Sutcliffe JS, Christian SL, Kubota T, Halley DJ, Meijers-Heijboer H, Langlois S, Graham JM Jr, Beuten J, Willems PJ, Ledbetter DH, Beaudet AL. The spectrum of mutations in UBE3A causing Angelman syndrome. *Hum Mol Genet*. 1999 Jan;8(1):129-35.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9887341>
- Greer PL, Hanayama R, Bloodgood BL, Mardinly AR, Lipton DM, Flavell SW, Kim TK, Griffith EC, Waldon Z, Maehr R, Ploegh HL, Chowdhury S, Worley PF, Steen J, Greenberg ME. The Angelman Syndrome protein Ube3A regulates synapse development by ubiquitinating arc. *Cell*. 2010 Mar 5;140(5):704-16. doi: 10.1016/j.cell.2010.01.026.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20211139>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2843143/>
- Lalonde M, Calciano MA. Molecular epigenetics of Angelman syndrome. *Cell Mol Life Sci*. 2007 Apr;64(7-8):947-60. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17347796>
- Matentzoglou K, Scheffner M. Ubiquitin ligase E6-AP and its role in human disease. *Biochem Soc Trans*. 2008 Oct;36(Pt 5):797-801. doi: 10.1042/BST0360797.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18793139>
- Moncla A, Malzac P, Livet MO, Voelckel MA, Mancini J, Delaroziere JC, Philip N, Mattei JF. Angelman syndrome resulting from UBE3A mutations in 14 patients from eight families: clinical manifestations and genetic counselling. *J Med Genet*. 1999 Jul;36(7):554-60.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10424818>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734398/>
- Singhmar P, Kumar A. Angelman syndrome protein UBE3A interacts with primary microcephaly protein ASPM, localizes to centrosomes and regulates chromosome segregation. *PLoS One*. 2011;6(5):e20397. doi: 10.1371/journal.pone.0020397. Epub 2011 May 25.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21633703>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3102111/>
- Tan WH, Bacino CA, Skinner SA, Anselm I, Barbieri-Welge R, Bauer-Carlin A, Beaudet AL, Bichell TJ, Gentile JK, Glaze DG, Horowitz LT, Kothare SV, Lee HS, Nespeca MP, Peters SU, Sahoo T, Sarco D, Waisbren SE, Bird LM. Angelman syndrome: Mutations influence features in early childhood. *Am J Med Genet A*. 2011 Jan;155A(1):81-90. doi: 10.1002/ajmg.a.33775.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21204213>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3563320/>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/UBE3A>

Reviewed: October 2011
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services